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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,349	12/19/2001	Yasuki Kato	5.1195	1803
5514	7590	03/23/2004	EXAMINER	
FITZPATRICK CELLA HARPER & SCINTO 30 ROCKEFELLER PLAZA NEW YORK, NY 10112			KISHORE, GOLLAMUDI S	
			ART UNIT	PAPER NUMBER
			1615	

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/018,349

Applicant(s)

KATO ET AL.

Examiner

Gollamudi S Kishore, PhD

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-5,8-12,16,19,20 and 22-41 is/are pending in the application.
- 4a) Of the above claim(s) 3-5,8-12 and 26-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16,19,20,22-25,35-39 and 41 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1-21-2003. 6) ☐ Other: _____

Art Unit: 1615

DETAILED ACTION

The affidavit dated 11-21-03 and the amendment dated 11-26-03 are acknowledged.

1. Newly submitted claims 3-5, 8-12 and 26-34 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

The original method claims were directed to the method of preparation of liposomes, whereas the newly presented claims are drawn to a method of inhibiting the leakage of drugs from the liposome preparations and thus, distinct from the original claims.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 3-5, 8-12 and 26-34 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims included in the prosecution are 16, 19-20, 22-25, 35-39 and 41.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -



Art Unit: 1615

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 16,19-20, 23, 25, 35, 37, 39 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Woodle (5,356,633).

Woodle discloses a method of preparation of multilamellar vesicles (MLVs) containing a drug. The liposome sizes are 160 nm. The drugs include both steroidal and non-steroidal anti-inflammatory agents and anticancer agent, methotrexate. The lipids used for the preparation of MLVs are PEG-DSPE, DPPC and DSPC (note the abstract, Examples, Example 4 in particular and claims).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant based on the amended claims, argues that Woodle's liposomes contain cholesterol. Applicant is incorrect in making this statement since Woodle teaches liposomes containing cholesterol and those containing no cholesterol (Table 3 and Example 7).

3. Claims 16, 19-20, 23, 25, 35, 37, 39 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Burke (5,552,156).

Burke discloses multilamellar vesicles and unilamellar vesicles containing the anti-cancer agents, camptothecins. The lipids include DSPC. Although Burke does not specifically state the sizes of liposomes since the preparations since he teaches both MLVs and SUVs, the amended liposome sizes are implicit (note the abstract, col. 6, lines 11-46 and Examples 4-6).

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant amends claims to delete cholesterol originally claimed and argues

Art Unit: 1615

that Burke teaches cholesterol. This argument is not found to be persuasive since Burke teaches both. The examples 1-3 contain no cholesterol at all.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

4. Claims 16, 19-20, 22-23, 25, 35-37, 39 and 41 are rejected under 35 U.S.C. 102

(a) or (b) as being anticipated by EP 0 850,646 of record.

EP discloses liposome formulations containing indolocarbazole derivatives. The liposomes are made from hydrogenated phospholipids and PEG-DSPE (note abstract, page 4, Examples and claims). Although, EP does not explicitly state that the liposomes are multilamellar, according the examples (example 1), the lipid film is hydrated and vortexed and not sonicated. Therefore, formation of multilamellar vesicles with sizes more than 120 nm is implicit.

The 102 (b) rejection will be reconsidered upon the review of the English translation of the Japanese priority.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant based on the amended claims, once again argues that EP discloses liposomes having cholesterol. Applicant is incorrect; the examples show no addition of cholesterol. Applicant further argues that a comparative experiment conducted show the liposomal sizes in EP are 1883 nm. This argument is not found to be persuasive for the following reason. Examples (1 and 22) of EP shows that the preparation is passed through 0.4 micron filters (400 nm). It is logical therefore, to

Art Unit: 1615

expect the sizes of the liposomes to be within the range claimed. The comparative experiment conducted by applicant does not show this filtration taught by EP.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 24 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodle cited above by itself or in view of (Mauer, BBA, 1998, 1374, pp., 9-20) of record.

As pointed out above, Woodle discloses a method of preparation of multilamellar vesicles (MLVs) containing a drug. The liposome sizes are 160 nm. The drugs include both steroidal and non-steroidal anti-inflammatory agents and anticancer agent, methotrexate. The lipids used for the preparation of MLVs are PEG-DSPE, DPPC, DSPC (note the abstract, Examples, Example 4 in particular and claims). Although Woodle does not teach the encapsulation of antibiotics or the claimed specific cancer drug it would have been obvious to one of ordinary skill in the art that any desired drug could be encapsulated within the liposomes based on the guidance provided by Woodle. One of ordinary skill in the art would be motivated further to encapsulate these compounds the reference of Mauer which teaches the knowledge in

Art Unit: 1615

the art of encapsulation of the antibiotic, ciprofloxacin in the liposomes (note the abstract). One of ordinary skill in the art would expect similar encapsulation.

7. Claims 22 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Woodle cited above in combination with EP cited above.

What is lacking in Woodle is the teaching of indolocarbazole derivatives as the active agent. However, it would have been obvious to one of ordinary skill in the art that any desired drug could be encapsulated within the liposomes based on the guidance provided by Woodle, especially in view of EP which teaches the knowledge in the art of encapsulation of this compound in the liposomes. One of ordinary skill in the art would expect similar encapsulation.

2. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Art Unit: 1615

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, PhD whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 1234.



Gollamudi S Kishore, PhD
Primary Examiner
Art Unit 1615

GSK